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In the Limelight: November 2021

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This month's feature highlights three articles that appear in the current issue of *Mayo Clinic Proceedings*. These articles are also featured on the *Mayo Clinic Proceedings*' YouTube Channel (https://youtu.be/p2YsRLmSxA0).

THE SIGNIFICANCE OF NEGATIVE SARS-CoV-2 MOLECULAR TESTING WITHIN 72 HOURS OF AIRLINE TRAVEL

Travel has the potential of spreading communicable diseases, and this is especially true for airline travel, with its relative proximity of passengers, the confines of the airline cabin, and speed and efficiency with which travellers are brought into contact with distant communities. Knowing whether a passenger has an active SARS-CoV-2 on a commercial airline fight is a critically important issue for both the infected passenger as well other passengers who would be at risk for acquiring the infection during travel. In the present issue of *Mayo Clinic Proceedings*, Tande et al evaluated the extent to which SARS-CoV-2 testing within a specific time frame before departure (within 72 hours) could aid in assessing such risk. These investigators studied passengers on commercial flights between the United States (departing either from JFK, New York City, or ATL, Atlanta) and arriving in Italy (FCO, Rome, or MXP, Milan). During the study period (December 19, 2020, through May 19, 2021), the average community infection prevalence rate was estimated at the time to be 1.1%. Individuals in this study were required to provide evidence of a negative molecular test result for SARS-CoV-2 within 72 hours of their departure and to confirm the absence of symptoms of COVID-19. Passengers then underwent a rapid antigen test and a rapid molecular test, if the former were positive. Patients with a positive molecular test were not allowed to board. In Italy, passengers were once more tested with a rapid antigen test, and a rapid molecular test, if the former were positive. In their analysis of 9,853 passengers who reported a negative SARS-CoV-2 PCR performed within 72 hours of departure either from JFK or ATL, 4 passengers tested positive by the rapid antigen test and molecular test at these airports, with one additional similarly positive passenger detected on arrival in Italy. The significance of this timely study by Tande and colleagues is at least two-fold. First, this logistically challenging study required collaboration among diverse groups, including, among others, Mayo Clinic, Delta Air Lines, the Georgia Department of Health, the Centers for Disease Control and Prevention (CDC), the relevant airports in the United States and Italy, and the Italian government authorities. Second, this novel study demonstrates that a quite low percentage of airline passengers, departing on an international flight, will be identified as having active SARS-CoV-2 infection on a rapid antigen test, if within the preceding 72 hours, these passengers had a negative SARS-CoV-2 molecular (PCR) test.

Tande AJ, Binnicker MJ, Ting HH, et al. SARS-CoV-2 testing before international airline travel, December 2020 to May 2021. *Mayo Clin Proc.* 2021;96(11):2856-2860.

DIAGNOSING CARDIAC AMYLOIDOSIS BY AN AI-ENHANCED ECG

For those diseases in which specific therapies may ameliorate their course and prognosis, it is especially important that their diagnosis be disclosed without delay, and, preferably, as facilely and as nonintrusively as possible. The standard electrocardiogram (ECG) is a relatively simple, straightforward, inexpensive, noninvasive, widely utilized diagnostic tool that is conventionally used in assessing arrhythmias, coronary artery disease, acute coronary syndromes, and ventricular hypertrophy and strain. In the present issue of *Mayo Clinic Proceedings*, Grogan et al demonstrate how the application of artificial intelligence (AI) can transform the standard ECG into a sensitive modality that may call attention to the presence of underlying cardiac amyloidosis, a disease usually diagnosed either by sophisticated noninvasive cardiac imaging or by an invasive cardiac biopsy. Cardiac amyloidosis is mainly caused by two conditions, namely, light chain-associated and transthyretin amyloid, the former a relatively rare disease, and the latter a diagnosis that is either missed or delayed and not as rare a disease as was once thought. Cardiac amyloidosis caused by either condition is a major determinant of morbidity and mortality, and not only can they both be treated, but improvements in such therapies are steadily evolving. The essential findings of Grogan et al are that the 12-lead ECG can reliably predict cardiac amyloidosis when enhanced by AI, and this is true for either type of cardiac amyloid; that when serial ECGs were available for AI enhancement, such prediction of cardiac amyloidosis may antedate the clinical diagnosis in the majority of cases; and, as remarkably, point-of-care screening and diagnosis can capitalize on this AI-enhanced ECG innovation because this technological advance can be adapted to single-lead and 6-lead data acquisition. As emphasized by Grogan et al, a major challenge that exists with regards to cardiac amyloidosis is that it is insufficiently considered and diagnosed by providers, thereby depriving patients with this disorder the timely institution of therapy that can ameliorate the course of the disease. The importance of this technologic advance by Grogan et al is manifold, and in particular, is its heightening of awareness and recognition of an underdiagnosed disease such that effective therapies can be expeditiously initiated.

Grogan M, Lopez-Jimenez F, Cohen-Shelly M, et al. Artificial intelligence-enhanced electrocardiogram for early detection of cardiac amyloidosis. *Mayo Clin Proc.* 2021;96(11):2768-2778.

CONSENSUS RECOMMENDATIONS ON MYALGIC ENCEPHALOMYELITIS/CHRONIC FATIGUE SYNDROME (ME/CFS)

This issue of *Mayo Clinic Proceedings* provides a consensus summary by Bateman et al of a poorly understood, underdiagnosed, quite challenging condition, namely, ME/CFS. This article is based on the knowledge, expertise, and experience of 21 clinicians dedicated to the study of this condition and its management. This article is timely not only because of the relatively high prevalence of ME/CFS and the burden imposed on those afflicted with this condition, but also because of the following considerations: 1) New evidence-based diagnostic criteria have been formulated by the National Academy of Medicine (and espoused by the Centers for Disease Control and Prevention [CDC]); 2) Management of ME/CFS is evolving as the understanding of ME/CFA increases, as, for example, time honored management approaches (graded exercise and cognitive-behavioral therapy) are no longer recommended by the CDC and other agencies; and 3) In the current COVID-19 pandemic, characteristics of ME/CFS are mimicked by the post-COVID-19 syndrome. Bateman et al discuss epidemiology, adverse effects and outcomes in ME/CFS, current diagnostic criteria, and pathophysiology. The latter

includes the functional significance and involvement of post-exertional malaise, unrefreshing sleep, cognitive impairment/neurologic abnormalities, autonomic dysfunction, altered immunity, and infectious processes. Key aspects of the history and physical examination are covered followed by recommended diagnostic tests. Management critically involves such essential strategies as validating the patient's symptoms and condition; assessing and supporting patient needs; educating the patient on the importance of pacing; appropriately addressing and treating symptoms, and, where relevant, co-morbidities; maintaining regular patient follow-up; and discussing short- and long-term prognosis. Importantly, the authors also discuss key conditions to be considered in the differential diagnosis as well as management approaches that were once recommended but are no longer advised. This invaluable synopsis of ME/CFS distills essential considerations in the diagnosis and management of this condition and will promote recognition of this relatively common disorder.

Bateman L, Bested AC, Bonilla HF, et al. Myalgic encephalomyelitis/chronic fatigue syndrome: essentials of diagnosis and management. *Mayo Clin Proc*. 2021;96(11):2861-2878.

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